Blood Purification

Blood Purif 2009;27(suppl 1):2–4
DOI: 10.1159/000213489

Published online: June 26, 2009

Worldwide Guidelines for the Preparation and Quality Management of Dialysis Fluid and Their Implementation

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Key Words
Hemodialysis · Fluid quality · Standards

Abstract
Quality standards for dialysis water have existed for more than 25 years. Current standards generally agree concerning the maximum allowable levels of chemical contaminants; however, significant differences exist concerning the maximum allowable levels of microbiological contaminants and the methods used to measure them. While quality standards for dialysis water are common, there are relatively few standards or recommendations for dialysis fluid quality and these also differ markedly in the maximum allowable level for microbiological contaminants. Compliance with quality standards for dialysis water and dialysis fluid appears to have improved over the past 20 years, although the actual extent of compliance is difficult to assess. A universal standard for fluid quality might be of benefit to the wider dialysis community; however, progress towards that goal will depend on resolution of important issues, including how the standard is to be applied, if it should be limited to substances with documented toxicity for hemodialysis patients, and how to address microbiological contaminants.

Quality Standards for Dialysis Fluid

It was recognized in the 1960s that both chemical and microbiological contaminants in dialysis fluid could cross the dialyzer membrane and injure patients. This recognition led to the development in the United States of standards for the chemical and microbiological quality of water used to prepare dialysis fluid and for the microbiological quality of the dialysis fluid. Subsequently, other national, regional and international bodies published similar standards for dialysis water quality [1].

The standards for the chemical quality of dialysis water encompass three broad categories of chemicals: (1) electrolytes that are normally included in dialysis fluid, with maximum allowable levels set so that dialysis water does not significantly affect the dialysis prescription; (2) chemicals with documented toxicity in dialysis patients, with maximum allowable levels set below those at which toxicity has been observed, and (3) trace elements regulated in drinking water, with maximum allowable levels generally set at one-tenth of those permitted in drinking water. There is widespread agreement between the various standards for dialysis water concerning the maximum allowable levels of chemical contaminants, with

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only minor differences in the selection of heavy metals and the maximum allowable levels for some of the electrolytes normally included in dialysate.

Current standards differ only slightly in the maximum levels of bacteria allowed in standard dialysis water; however, there are important differences in the methods used to determine those levels. In particular, the combination of culture medium, incubation time and incubation temperature specified in the United States standard yields significantly lower levels of bacteria than those obtained using the conditions specified in the European Renal Association's Best Practice Guidelines [2]. Apart from differences in determining levels of bacteria, there are also significant differences in the maximum allowable levels of endotoxin, which range from 2 EU/ml in the United States to 0.05 EU/ml in Japan.

While there are many quality standards for dialysis water, there are fewer standards for dialysis fluid, which is ultimately what the patient is exposed to during a dialysis treatment. In general, quality recommendations for standard dialysis fluid are the same as the corresponding recommendation for dialysis water. Some organizations, such as the European Renal Association, go beyond standard quality fluids and recommend that ultrapure dialysis fluid, defined as containing <0.1 CFU/ml and <0.03 EU/ml of endotoxin, be used for all dialysis treatments. This recommendation is made in view of a growing body of evidence that use of ultrapure dialysis fluid is associated with a reduction in many of the complications associated with hemodialysis therapy [3].

Implementation of Quality Standards

Surveys of dialysis fluid quality from the late 1980s show that many dialysis facilities did not comply with applicable standards for microbiological quality [4, 5]. Changes in compliance since that time can be difficult to assess because of differences in how standards are implemented. For example, while the standards for microbiological quality are least strict in the United States, dialysis facilities are required to meet them in order to receive payment from the Federal Government and compliance is monitored by regular inspections of the dialysis facilities. In contrast, many European countries, such as Italy, recommend the use of ultrapure fluids, but there is no requirement that this level of purity be met and no inspection for compliance. While published reports provide some information on compliance with fluid quality standards they are generally based on self-reported levels of contamination and do not include data from all facilities or even a properly constructed statistical sample of facilities. Moreover, monitoring of fluid quality may be infrequent or not performed [6, 7]. With those caveats, it appears that compliance with current standards has improved over the past 20 years. For example, 70–90% of small samples of centers from Austria [8] and Italy [7] are reported to comply with applicable standards for bacteria, while more than 97% are reported to comply in a large sample of centers from Japan [6].

Where Next with Quality Standards?

In view of the proliferation of standards over the past few years, it may be time to consider how to harmonize existing standards into a single standard that would be widely applicable in all hemodialysis settings. Such a universal standard would aid in comparing outcomes between different countries and regions and provide a sound basis for spreading best practices to regions with less mature dialysis programs. Current efforts by the International Organization for Standardization (ISO) to develop a series of standards and guidelines for dialysis fluids represent one effort in this direction. Important issues remain to be resolved, however. First, a universally applicable standard must take into account how the standard is to be applied – as a mandatory regulation or a goal to be aspired to. Second, it is not practicable to continue adding trace elements to the standard as they are added to drinking water standards if there are no data to document specific toxicity for hemodialysis patients. Third, differences in bacterial culturing methods must be resolved, most likely in favor of the most rigorous methods, and a decision must be made whether or not to include other microorganisms, such as yeasts and fungi, and bacterial products not detected by the *Limulus* amebocyte lysate assay. Finally, in spite of the universal availability of quality standards for dialysis fluids, relatively little information is available to dialysis practitioners to guide them in the successful implementation of those standards. The Association for the Advancement of Medical Instrumentation (AAMI) published a recommended practice for dialysis fluids in 2004 [9] and some information is also provided in the European Renal Association's Best Practice Guidelines [10]. However, neither of these documents provides detailed guidance on the implementation of ultrapure fluids. A guidance document (Guidance for the preparation and quality management of flu-

ids for haemodialysis and related therapies) currently being developed by ISO and expected to be available in 2010 will, at least in part, address this absence of information.

Disclosure Statement

The author is convener of the ISO Working Group on renal replacement, detoxification and apheresis (ISO/TC 150/SC 2/WG 05). The opinions expressed in this article are those of the author and do not necessarily represent the position of ISO or the ISO Working Group.

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